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**Regulation of collagenase-3 expression in human breast carcinomas is mediated by stromal-epithelial cell interactions.**

Uria JA, Stahle-Backdahl M, Seiki M, Fueyo A, Lopez-Otin C

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Collagenase-3 (MMP-13) is a recently identified member of the human matrix metalloproteinase gene family that is expressed in breast carcinomas and in articular cartilage from arthritic patients. Here, we have studied the cellular origin of this enzyme in breast carcinomas by in situ RNA hybridization, and we found that collagenase-3 is expressed by stromal cells immediately adjacent to epithelial tumor cells but not by the tumor cells themselves; nor is it expressed by the normal breast glandular epithelium. Consistent with this observation, coculture experiments using human fibroblasts and MCF-7 breast cancer cells revealed that conditioned medium from breast cancer cells stimulated the fibroblastic expression of collagenase-3 mRNA. In contrast, no stimulatory effect was observed when medium from fibroblast cells was added to breast cancer cells. These results strongly suggest that transcription of collagenase-3 in stromal cells is activated by diffusible factors released from epithelial breast cancer cells. A survey of a series of cytokines and growth factors known for their ability to induce collagenase-3 expression in human fibroblasts identified interleukin-1alpha and interleukin-1beta as potential candidates for inducing the expression of this MMP gene in breast carcinomas. According to these results, collagenase-3 should be included among the molecular factors that are detected during the stromal reaction to invasive breast cancer and that, by concerted action, may be essential for tumor growth and progression.

PMID: 9354453, UI: 98014576

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